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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/780,532	02/09/2001	Clive Wood	GNN-012CP	8383
7590	08/29/2008		EXAMINER	
Ivor R. Elrifi MINTZ LEVIN COHEN COHN FERRIS GLOVSKY AND POPEO PC One Financial Center Boston, MA 02111			QIAN, CELINE X	
			ART UNIT	PAPER NUMBER
			1636	
			MAIL DATE	DELIVERY MODE
			08/29/2008	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Advisory Action Before the Filing of an Appeal Brief</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/780,532	WOOD ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	CELINE X. QIAN	1636

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 11 August 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1.  The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

a)  The period for reply expires 6 months from the mailing date of the final rejection.  
 b)  The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2.  The Notice of Appeal was filed on 11 August 2008. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3.  The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
 (a)  They raise new issues that would require further consideration and/or search (see NOTE below);  
 (b)  They raise the issue of new matter (see NOTE below);  
 (c)  They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
 (d)  They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4.  The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5.  Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.

6.  Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7.  For purposes of appeal, the proposed amendment(s): a)  will not be entered, or b)  will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: \_\_\_\_\_.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8.  The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9.  The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10.  The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11.  The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.

12.  Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_

13.  Other: \_\_\_\_\_.

/Celine X Qian Ph.D./  
 Primary Examiner, Art Unit 1636

Continuation of 11. does NOT place the application in condition for allowance because: the argument directed to the 112 1st paragraph is not persuasive. In response to the new matter rejection, Applicants cites specification on pages 8, line 29 through page 9, line 5, and page 11, lines 1-14 to support the method of modulating proliferation of a cell by contacting the cell with an agent that modulates the expression or activity of a TRADE family polypeptide in which the cell possesses TRADE activity. Applicants further cites page 19, line 18 through page 25, line 2 to support the claimed method. Applicants argue that based on the teaching from these passages and the originally filed claims 15, 16, 18-20 and 25, it would be clear to one of skill in the art only cells with TRADE activity will respond to the administration of an extracellular portion of the TRADE polypeptide, thus the claimed method has adequate description from the specification. The arguments have been fully considered but deemed unpersuasive. The teaching from the cited passages have been carefully considered, but the collective teaching of the cited passages does not support the notion that the claimed method has adequate description. The passage from page 8-9 describes the expression of TRADE in various tissues, whereas the teaching from pages 11 addresses describes what "trade activity" encompasses. The teaching from pages 19-25 describes a number of ways for modulating TRADE expression and activity, including using antisense for inhibition of the expression, or stimulating TRADE activity by transfecting cells with expression vectors that expresses TRADE or contacting cell with TRADE protein (see pages 20, 2nd and 3rd paragraph). All these teaching does not address whether the method of modulating activation of an NFkB signaling pathway in a cell already having TRADE activity. Moreover, one of skilled in the art would recognize that stimulating TRADE activity may be accomplished by transfecting a cell that does not have TRADE activity with an expression cassette. Furthermore, claim 2 recites contacting cell with a soluble form of TRADE polypeptide that comprises the extracellular domain of a TRADE polypeptide, which is not limited to the extracellular portion of TRADE polypeptide. As such, the argument of only cells with TRADE activity will respond to the administration of an extracellular portion of the TRADE polypeptide is irrelevant. The agent that stimulates the expression of the TRADE transcription also does not require the cell to possess TRADE activity. Therefore, for reasons given in previous office action and above, this rejection is maintained.

In response to the enablement rejection, Applicants argue that the specification teaches a number of TRADE polypeptides and fusion peptides including TRADE 1-368, 1-328, 1-218, 1-196. Applicants argue that the collective teaching from the specification and the prior art enables the claimed invention. The argument has been considered but deemed unpersuasive. All the fragments of TRADE mentioned above are longer than that of 1-168 of SEQ ID NO:2. The specification fails to demonstrate a soluble form of TRADE polypeptide that encoded by a polynucleotide 98% homologous to the polynucleotide encoding 1-168 amino acid of SEQ ID NO:2 that functions as an antagonist of a TRADE ligand, and thereby modulates the NFkB activation in all cell type in vitro or in vivo. Neither example 4 nor any other portion of the specification demonstrates that such a soluble TRADE polypeptide can change the activity of the intracellular portion of the TRADE protein. While Figure 14 and Example 11 describes the effect of a number of TRADE deletion mutant on the activation of NFkB signaling, it does not show that a soluble polypeptide encoded by a polynucleotide at least 98% to the polynucleotide encoding 1-168 of SEQ ID NO:2 affects or antagonizes the TRADE ligand activation of NFkB signaling pathway because transfection of pcDNA3 and TRADE1-198 has similar effect on the reporter assay. Therefore, for reasons given in the previous office actions and above, the written description rejection and enablement rejection are maintained.